IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

WENDY B. DOLIN Individually and as Independent Executor of the Estate of STEWART DOLIN, deceased,	No. 12 CV 6403
Plaintiff,	
vs.	Chicago, Illinois
SMITHKLINE BEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, a Pennsylvania Corporation,	April 6, 2017
Defendant.	9:20 o'clock a.m.

VOLUME 15 A
TRANSCRIPT OF PROCEEDINGS
BEFORE THE HONORABLE WILLIAM T. HART

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(The following proceedings were had out of the presence of the jury in open court:)

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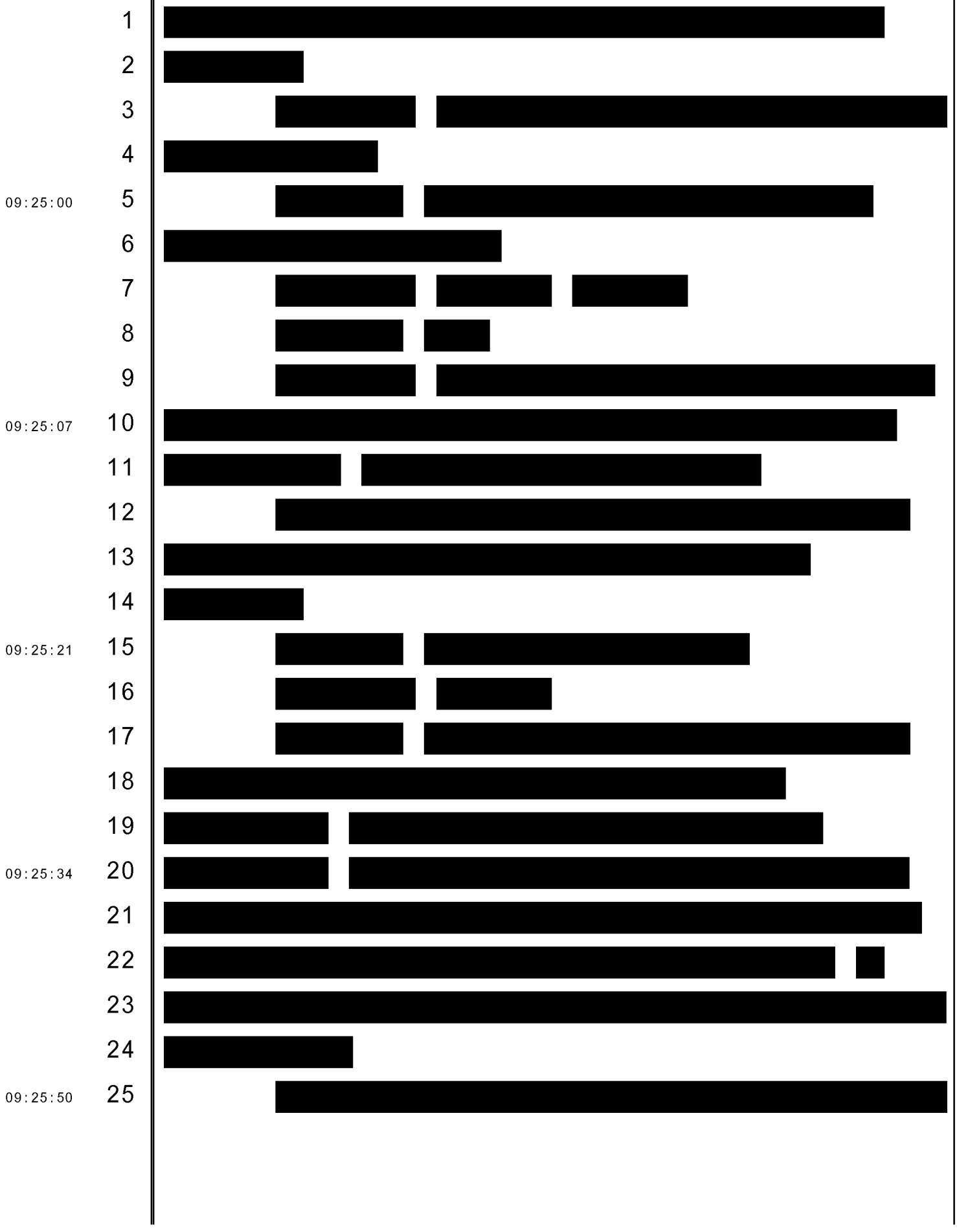
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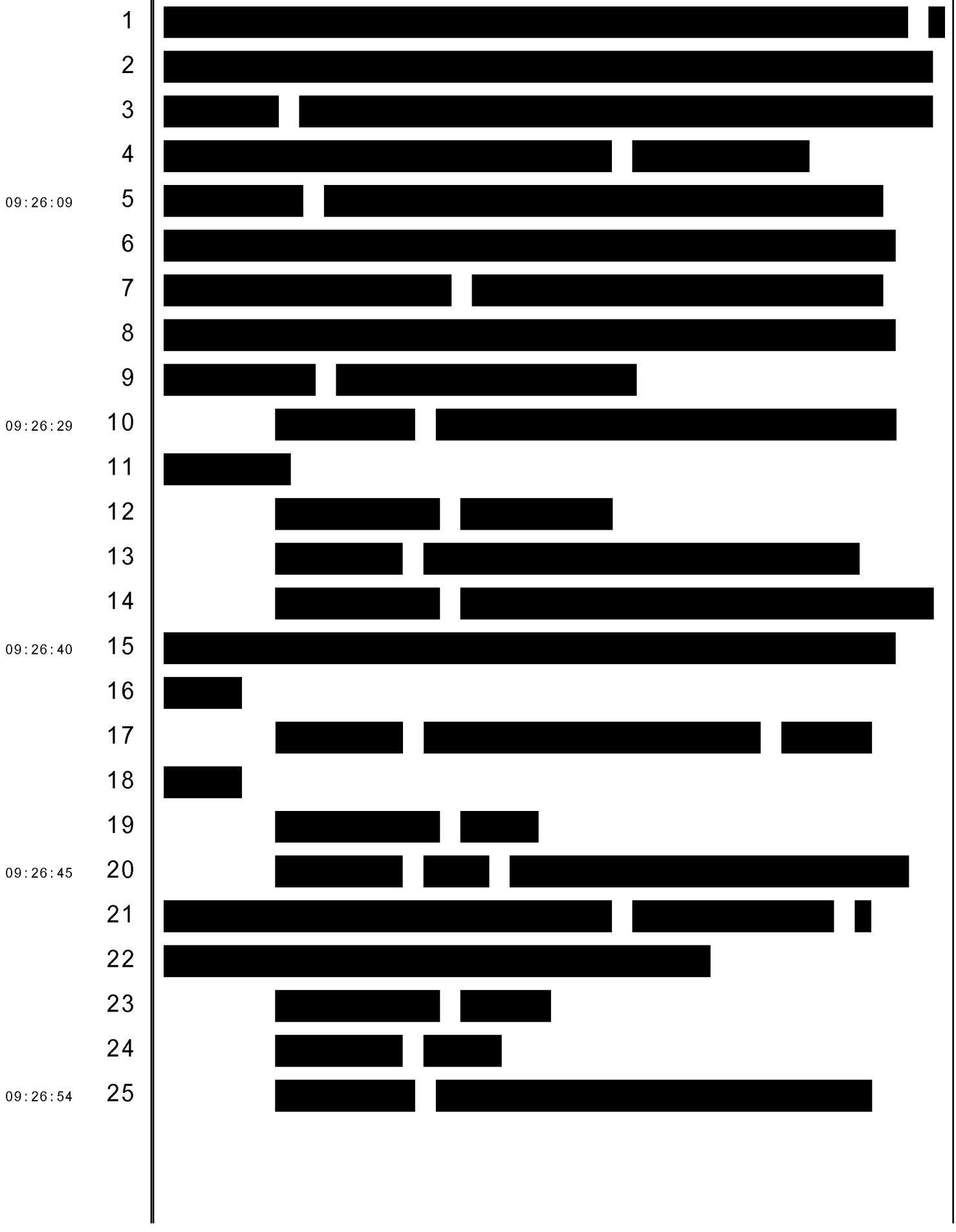
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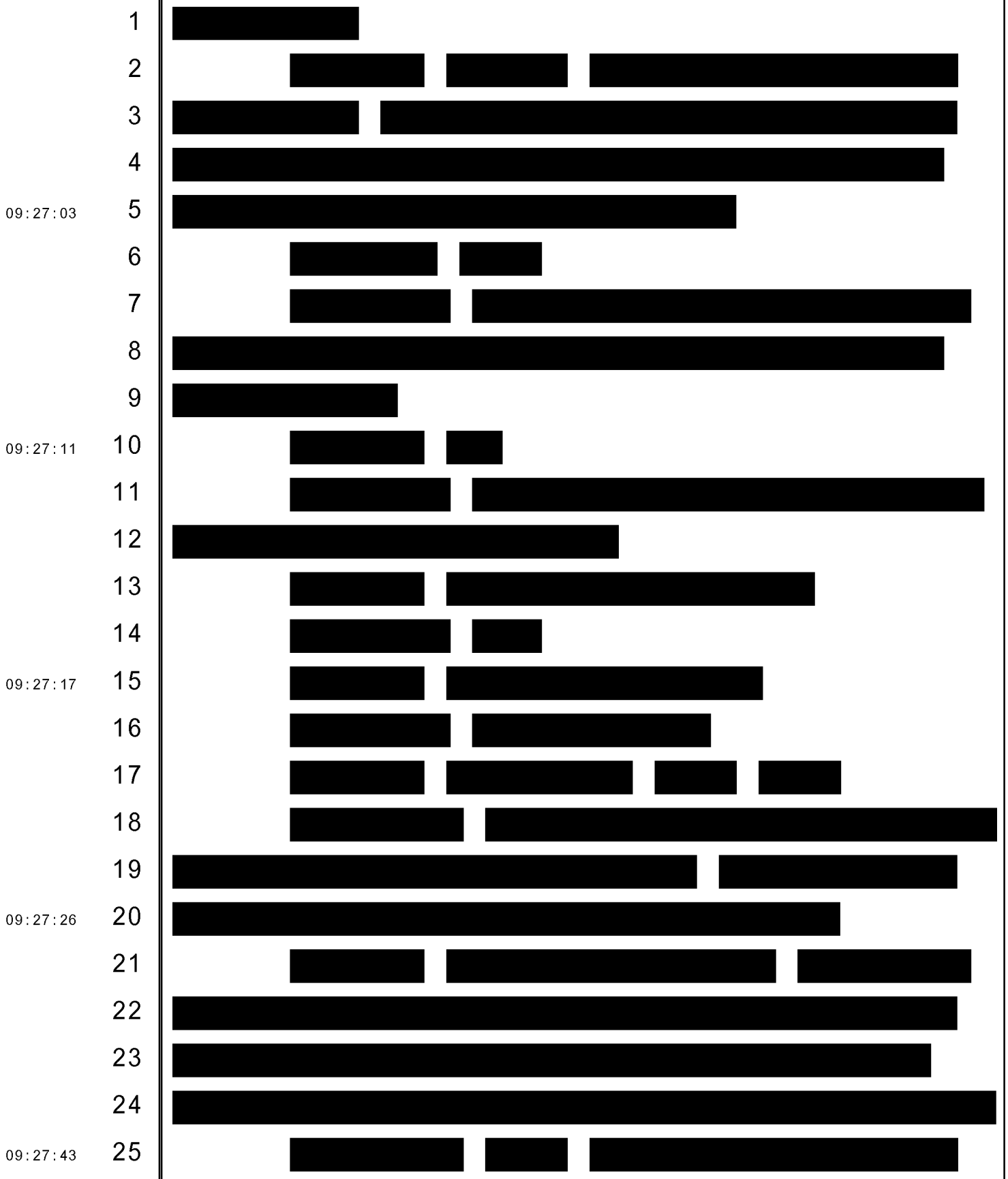
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09:28:13 (The following proceedings were had in the presence of the jury in open court:)

THE COURT: All right. Thank you very much, ladies and gentlemen. Please be seated. We will resume.

We will continue today to listen to and hear 09:29:18 depositions which have been taken in this case.

Now I want to tell you that we worked on these depositions in the sense that the lawyers have reasonably eliminated a lot of the material, and I have eliminated some of it myself.

09:29:34 So I know it's not easy to listen to this material or any material that's shown and read to you. You've been very good and I thank you for it, but I assure you that we're trying very much to cut down as much as possible, both sides are cooperating very well, to eliminate it.

09:29:55 So I call upon you again for your great patience which we appreciate.

All right. You may proceed.

MR. BAYMAN: Thank you, Your Honor.

09:30:07

(Whereupon, videotape deposition of John Iino played in open court).

MR. BAYMAN: We would call now by video David DeNinno.

THE COURT: All right. Proceed.

09:47:38 (Videotape deposition of David DeNinno played in open court, resumed)

MR. BAYMAN: One more short one, Your Honor. It's Mr. Jaskot.

THE COURT: All right. How long is this one?

10:33:09 MR. BAYMAN: 25 minutes.

THE COURT: All right. Proceed.

(Videotape deposition of Paul Jaskot played in open court)

THE COURT: Does concludes it?

10:58:31 MR. BAYMAN: Yes, sir.

THE COURT: Okay. Good time for our recess, ladies and gentlemen.

And who's next?

MR. BAYMAN: Dr. John Kraus, Your Honor.

10:58:45 THE COURT: Okay.

(The following proceedings were had out of the presence of the jury in open court:)

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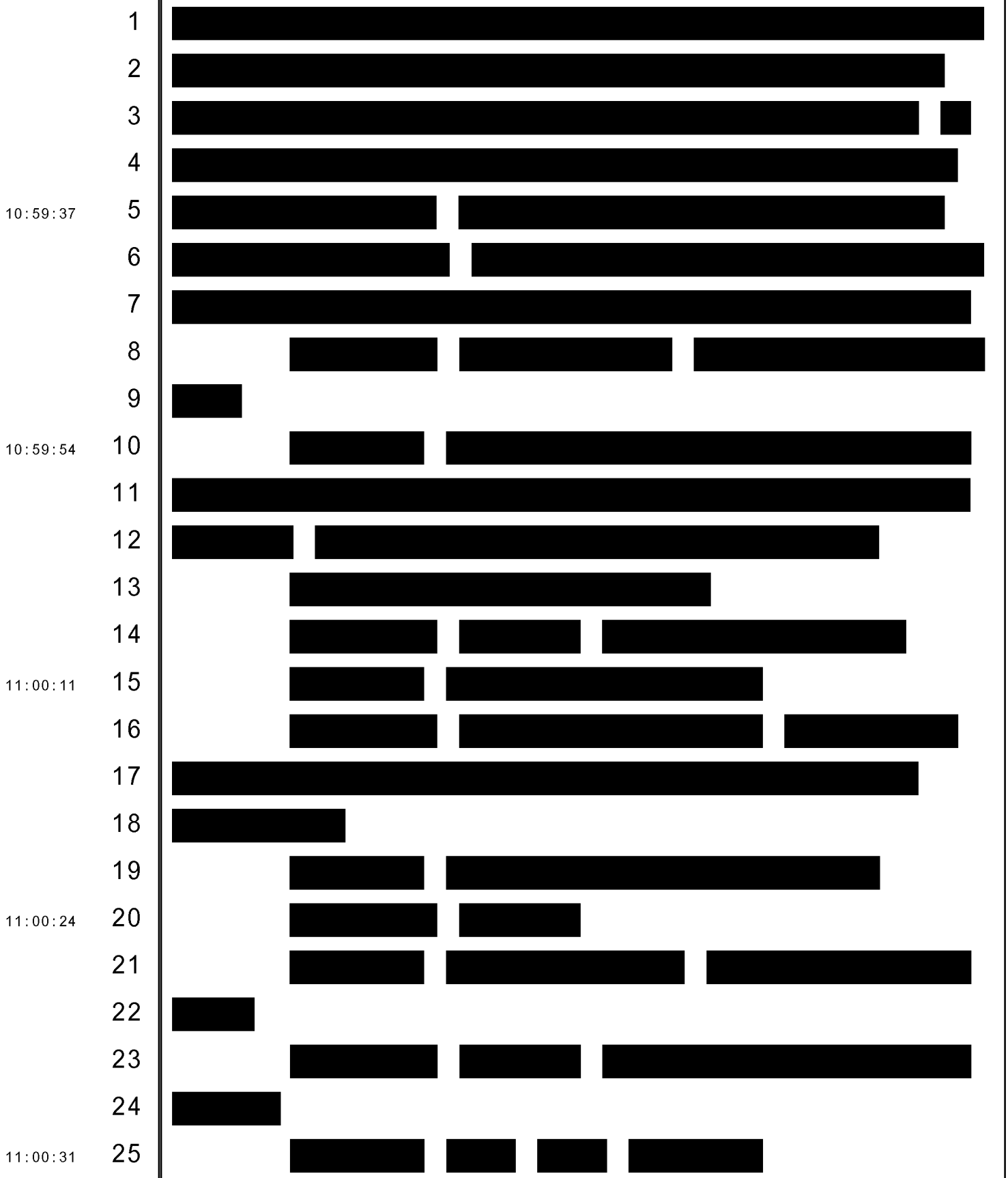
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(The following proceedings were had in the presence of the jury in open court:)

THE COURT: All right. Thank you very much, ladies and gentlemen. Please be seated.

We will resume.

MR. BAYMAN: Your Honor, we call John Kraus.

MS. HENNINGER: He'll be here shortly, Your Honor.

(Brief pause).

11:19:31 THE COURT: All right. Sir, step up here, please (indicating).

Around there, if you will (indicating).

Please raise your right hand.

(Witness duly sworn.)

11:19:48 THE COURT: You may take the witness stand.

THE WITNESS: Thank you.

THE COURT: You may proceed.

Please read the credentials to the jury.

MR. BAYMAN: Yes, Your Honor.

11:19:59 Dr. John Kraus is currently Vice President and Medicine Development Leader at GlaxoSmithKline.

He obtained his Bachelor's Degree at the University of Florida, graduating with high honors.

He obtained a medical degree, as well as a Ph.D. in 11:20:11 neurobiology from Duke University.

Dr. Kraus went on to a psychiatry residency at the University of North Carolina in Chapel Hill.

He is board certified in psychiatry by the American Board of Psychiatry and Neurobiology.

11:20:33 He is the author of over 20 peer-reviewed

publications, as well as several book chapters. He is a distinguished fellow of the American Psychiatry Association and a member of the Society of Biological Psychiatry.

Since 2013, Dr. Kraus has served as an external oversight board member of the network for excellence in neuroscience clinical trials.

JOHN KRAUS, DEFENDANT'S WITNESS, SWORN

DIRECT EXAMINATION

BY MR. BAYMAN:

11:21:00 Q. Good morning, Doctor.

A. Good morning.

Q. Please introduce yourself to the jury.

A. As you heard, my name is John Kraus. Nice to meet you.

Q. Where do you currently work, Dr. Kraus?

11:21:10 A. I work at GlaxoSmithKline based in RTP, North Carolina.

Q. Where in North Carolina?

A. In research Triangle Park.

Q. Is that near Raleigh?

A. Yes, that's near Raleigh.

11:21:30 Q. How long have you worked at GlaxoSmithKline?

A. Since November of 2005.

Q. The jury has heard a little bit about your education and your medical training.

Were you -- when you were at the University of North

11:21:47 Carolina at Chapel Hill doing your residency, were you involved

in any clinical trials?
A. Yes, I was. I was associate director of the clinical research unit where we conducted clinical trials.
And I apologize for the feedback.
11:22:12 (Noise interruption)
BY MR. BAYMAN:
Q. And the clinical trials that you were involved in, did they involve psychiatric medications?
A. Yes, they did.
11:22:21 Q. And did you have to evaluate patients using a term the jury has heard called rating scale?
A. Yes. In the psychiatric studies, in order to have consistent measurement between different doctors and different clinicians we use something called rating scales.
11:22:43 Q. Explain to the jury what a rating scale is.
A. It depends, they're specific for each disease, but typically they break down different symptoms of the disease, and oftentimes have kind of a numeric anchoring system. So, say a zero to 4, where a zero might be no evidence of that
11:23:05 symptom, and a 4 could be very bad.
And depending on the rating scale, those can be added up. So typically the higher the score, the more symptoms or the sicker a person is.
And they have specific ones for depression, for
11:23:21 schizophrenia, for bipolar disorder, things of that nature.

Q. And in the clinical trials that you worked on, did you have to monitor patients for adverse events?
A. Yes.
Q. And did you have to make some kind of assessment as an
11:23:40 investigator whether the adverse event was related to the study medication the patient was taking?
A. Yes; we were asked to do that.
Q. Did you conduct clinical trials that were your own trials?
A. Yes, I did.
11:23:57 Q. And did you conduct clinical trials that were sponsored by a pharmaceutical company?
A. Yes, I did.
Q. And at the University of North Carolina as an institution performing clinical trials, were you and your colleagues
11:24:14 subject to federal regulations and other rules that govern the conduct of those trials?
A. Yes; absolutely.
Q. And have similar rules and regulations applied to the investigators and the institutions that GlaxoSmithKline has
11:24:29 engaged to participate in GSK's sponsored clinical trials?
A. Yes; all investigators have to comply with regulations.
Q. And were any of the clinical trials that you were involved with, did they -- at the University of North Carolina, did they involve GlaxoSmithKline?
11:24:45 A. Yes.

Q. Have you had any formal education in statistics?
A. Yes, I have.
Q. Do you have experience performing statistical calculations and analyses as part of your research?
11:25:02 A. Yes, I have, both in my graduate school and in my clinical trials.
Q. Have you actually ever done statistical analyses for any published articles?
A. Yes, I have.
11:25:17 Q. About how many times?
A. I don't know. 7 or 8 or so.
Q. You authored an article in the journal of neuropsychology and clinical neuroscience?
A. Neuropsychiatry and clinical neuroscience, yes.
11:25:33 Q. And is that an article that's read by experts in your field?

MR. WISNER: Objection. Speculation.

THE COURT: Overruled.

BY THE WITNESS:
11:25:40 A. Yes, that's particularly for what are called neuropsychiatrists who kind of bridge neurology and psychiatry, which is some of the work I've done.
BY MR. BAYMAN:
Q. And did you do the statistical work for that article?
11:25:54 A. I did.

Q. Tell us a little bit about that.
A. I think the article you're referencing is sort of an observational study we did on the effect of a drug called clozapine on violent behavior in patients.
11:26:11 And, basically, the statistical assessment I performed for that paper was, looking at the time before and the time after the drug had started in these individuals; was there a decrease in the amount of violent behaviors.
And so using the test to show whether or not that
11:26:32 could've been chance or whether it was likely related to the treatment.
Q. Have you authored an article in a journal called Schizophrenia Research?
A. Yes.
11:26:42 Q. And did you do the statistical work for that article?
A. Yes.
Q. Have you authored an article in the Journal of Neuroscience in 1994?
A. Yes.
11:26:51 Q. And did you do the statistical work for that article?
A. Yes, I did.
Q. As a medical doctor, have you necessarily had to become knowledgeable about statistical methods used in medical literature?
11:27:04 A. You have to be knowledgeable, generally, about the meaning

of statistics in order to be able to interpret the medical literature.

In the method section of papers that are published in the literature, they'll talk about the statistical test used, and that gives you an idea of how to interpret the data that are in the paper.

Q. And as a medical doctor, have you necessarily had to become knowledgeable in statistical analyses that are presented in prescribing information and what the jury has heard called the label for prescription of medicine?

A. Yes; for first-time label, that's correct.

Q. And as a medical doctor, have you necessarily become knowledgeable about statistical analyses in reports issued by government agencies like the FDA?

A. Yes.

Q. And in your work at GlaxoSmithKline, have you participated in making decisions about which statistical methods will be used when analyzing different types of data?

A. Yes. At GlaxoSmithKline, as you might imagine, we have experts in statistics that we collaborate with, but they work with me as the physician and the clinical team to understand what is the problem we're looking at, what are we trying to understand, what are the data that come in, and then we collaborate together to understand how might we then use statistical test to see whether or not our idea is -- is due to

chance or is real.
Q. As a medical doctor, do you look at the statistical results and apply your medical judgment to them to determine whether there's any clinical significance what you might see?
11:28:45 A. Yes, I do.
Q. And do you also as a medical doctor and in your work at GSK, have you described statistical results to the medical community in reports, or in a label, or in a letter?
A. Yes, I've described statistical outcomes in addition to
11:29:04 those also in presentations or conferences.
Q. The jury obviously heard that you did your residency in psychiatry at the University of North Carolina. What was your first job after you finished your residency?
A. When I completed my residency I remained on faculty at the
11:29:26 University of North Carolina as an assistance professor of psychiatry.

And at the University of North Carolina we collaborated with at that time the largest state hospital, which was called Dorothea Dix Hospital. So I worked over at
11:29:41 Dorothea Dix, and one of my first responsibilities there was starting something we called the Crisis Stabilization Unit where every male patient admitted to the hospital was screened and evaluated in that unit, about 2,000 per year. And working with residents and medical students from the University of
11:30:00 North Carolina in that setting, as well.

Q. Did you have while you were in the faculty of North Carolina, did you have teaching responsibilities?
A. Yes; I was also the Associate Director of Residency Training. And when you start residency, a psychiatry residency
11:30:16 is 4 years, so the first year is what's called the intern year. So they come from medical school and they're coming to learn how to be a psychiatrist and take care of patients full time.

That group of students are residents. I was actually responsible for their oversight, and actually taught a course
11:30:38 throughout the year on all aspects of psychiatric treatment, diseases, medicines, to try to help them navigate that first year to be successful.
Q. And while you were on the faculty in North Carolina, did you have clinical research responsibilities?
11:30:58 A. Yes. So you see in academia, you have a lot of different titles. I was also the associate director of the Clinical Research Unit. And the Clinical Research Unit was based at Dorothea Dix Hospital, part of the reason I was there. It was a stand-alone clinical unit where we can house patients that
11:31:20 were participating in clinical trials.
Q. Tell the jury about the kinds of patients you treated at Dorothea Dix Hospital.
A. Right. So Dorothea Dix Hospital is or was a large state hospital. And it could include at that time admissions for
11:31:40 almost any kind of psychiatric condition, but it was really

designed for taking care of patients long term. So, weeks to months at a time. Very severe ill patients in that setting.

However, we had 3,000 admissions a year, 2,000 of them were men. So the reason we had started that unit that I have described, was to really evaluate and screen those who could be treated relatively acutely or quickly and then out to community care, and evaluate those who would need longer-term treatment.

So we had, literally, any sort of psychiatric condition you can imagine: Depression, suicide attempts, suicidal ideation, schizophrenia, psychosis, mania, et cetera, and substance abuse as well.

Q. Did you treat patients with anxiety?

A. Yes.

Q. Now, were you involved in any clinical trials?

A. Yes.

Q. Tell the jury about those, please.

A. We were involved in several clinical trials via our Clinical Research Unit. At the time I was associate director, the director was Jeff Lieberman who is now chairman at Columbia University in New York. And we were interested in schizophrenia research. So most of the studies that we had done at the Clinical Research Unit were around schizophrenia.

My colleague Brian Shiekman (phonetic) and I also did some research on violent behavior in our hospital, as you heard about with one of those manuscripts.

Q. Now, you said some of your patients were at high risk of suicide. Did you also treat patients who had more mild forms of anxiety and depression?
A. Yes. As I said, we screened thousands of patients each
11:33:34 year. Many of those patients had conditions that could be treatable with medications that did not require hospitalization and could require follow-up in the community. So more mild to moderate anxiety, depression, we did see, but we didn't have those patients stay in the hospital long. They didn't require
11:33:55 that level of care.
Q. Now, in addition to your research, did you actually treat the patients?
A. Yes.
Q. You were their physician?
11:34:01 A. Yes.
Q. Did you prescribe medicines to treat their depression and anxiety?
A. Oh, yes.
Q. What kind of medicines do you prescribe?
11:34:10 A. Whatever is available. When we are dealing with this population, that can be very difficult. Every sort of psychopharmacological medication we would use.
For depression in particular, typically we would use, you probably heard, SSRIs, or selective serotonin reuptake
11:34:31 inhibitors, but we would also use next uptake inhibitors and

other newer, as well as even real old antidepressants, depending on the patient that we were dealing with.
Q. Prior to going to work for GSK, did you ever prescribe Paxil to patients that you treated?
11:34:50 A. Yes.
Q. Now, in addition to your other responsibility, did you actually teach interns and residents about basic principles of psychiatry?
A. Yes. As I said, first year, every week, they had to meet
11:35:06 with me on Wednesday where we have a topic at hand that went all the way from we'd start with really emergency psychiatry, because that might be what they're faced with early, from history of psychiatry all the way to neurobiological changes with psychotherapy, for example.
11:35:25 Q. How long did you serve as assistant professor at the University of North Carolina?
A. Let's see. About 4 and a half years, 5 years.
Q. Okay. And then after leaving University of North Carolina, what did you do next?
11:35:40 A. That's when I joined GlaxoSmithKline in their neurosciences development center.
Q. What year was that?
A. 2005.
Q. Why did you decide to join a pharmaceutical company like
11:35:53 GSK?

A. Right. It was a tough decision, because as you might imagine, one thing I enjoyed is really working directly with patients, but what you also could see when, you know, working at a large hospital is, the treatments were limited and some
11:36:11 patients would come in over and over again, not taking their medicine or not having a good response.

And when I was thinking about where the real differences could be made and looking at my field of psychiatry, kind of two things in my view that really made a
11:36:28 good contribution to outcomes with patients with mental illness:

One is, obviously, medicines, and those medicines have been development by the pharmaceutical industry.

And the other is what I consider epidemiology and
11:36:45 actually better defining the disease from how it's characterized by symptoms but also by its genetics.

For me, given my background in neuroscience and clinical research, going into drug development was a logical next step, and that's why I did that.

11:37:02 Q. The jury has heard the term "epidemiology." What does that mean?

A. Epidemiology is kind of the study of the sort of natural existing characteristics of a disease or condition.

So, for example, what is its distribution across ages,
11:37:23 what is its distribution across the world, what is its outcome

over time, things of that nature. So, you kind of understand the basic characteristics of what happens with the disease.

And that's really important when you're trying to figure out are there certain points in the course of an illness where you might be able to make a bigger difference.

So treating something earlier might be better than treating something when the symptoms are pretty severe, for example.

Q. Now, even after moving to GSK, have you continued to work with students at the University of North Carolina?

A. Yes, I have.

Q. Tell us about that.

A. So, I'm still an adjunct professor at the University of North Carolina California. And what I have done is gone to the units, the clinical units, and sit with the students for what we call difficult case conferences.

So these were patients that they were having continued questions about; what is the diagnosis, what is the best treatment. And I would interview the patient with the resident, the medical student, and then we would talk about different options, what could be done, things that maybe they didn't consider, and also different diagnostic options that they may not have considered as well.

Q. You mentioned that the area you joined at GlaxoSmithKline was called the neurosciences therapy area.

A. Back then it was called Neurosciences Medicine Development Center, but names get changed all the time. Right now it's called the Neurosciences Therapy Area Unit.
Q. What does that part of the company do?
11:39:05 A. That part of the company develops medicines for neurologic and psychiatric disorders.
When I joined the company in 2005, there was a large discovery program in psychiatric disorders. So I started working on new medicines for depression, anxiety, and
11:39:31 schizophrenia when I joined the company.
We also have medicines for neurologic conditions. And right now, in 2017, we're really focused on looking at certain kinds of neurodegenerative disorders, like Alzheimer Disease and Parkinson's Disease.
11:39:50 Q. And your work in what you call drug development, did that include designing clinical studies?
A. Oh, yes.
Q. And would that include then capturing data about the effectiveness of a drug and safety of a drug?
11:40:13 A. Yes, it does.
Q. And you were -- I'm going to talk to you a little bit about what else you've done, but as part of your job responsibilities, were you promoted?
A. Yes.
11:40:32 Q. Tell the jury about that.

A. So, in terms of the different roles and position I've had?
Q. Yes.
A. Okay. So, when I started at the company I was what's called Director of Medical Sciences. So, I was the physician on the team that was really responsible for making sure that the study designs or protocols were appropriately measuring the right things to understand the outcome, and also ensuring that the patient's safety was maintained throughout the study.

The next step was getting promoted to senior director where you're doing the same thing, you just have the "senior" in front of the title.

And then after that, though, I became promoted to Head of Medical Sciences in Neurosciences where the physicians in psychiatry and neurology reported in to me and I managed their activities across all the projects, and managed their development to ensure they were getting their career goals met.

And the next step was promotion to Head of Medical Governance in the neurosciences therapy unit where I was still having the physicians from the United States, from England report in to me, and also the physicians -- we had a site in Shanghai China would report in what we call dotted line. I wasn't their direct manager, but was responsible for ensuring that their projects going well.

But I also was responsible for a couple of other things. We had an internal peer review where every protocol,

every project had to be reviewed and to ensure that it was appropriate to understand the outcome, the Alzheimer Disease, Multiple Sclerosis, or some other disorder, and to make sure, that the medical governance perspective, that we were
11:42:33 maintaining the safety of the patients.

So, I actually chaired that peer-reviewed. Had very interesting meetings at about 5:00 a.m. in the morning at RTP so we could have our Shanghai colleagues join by video conference.

11:42:48 MR. WISNER: Your Honor, I'd ask that -- this is all stuff that happened well after 2010, and while it is, interesting, Doctor, I don't mean any disrespect, could we get this moving along to Paxil?

THE COURT: Let's get right to the case.

11:42:59 MR. BAYMAN: Okay.

THE COURT: I've asked you to condense that. We know the doctor has credentials. Let's get right to the case.

MR. BAYMAN: Well, that's actually where I was turning, Your Honor.

11:43:08 BY MR. BAYMAN:

Q. As part of your work, you said you worked on developing new medicines, did you support medicines that had already been approved like the medicine at issue in this case, Paxil or Paroxetine?

11:43:20 A. Yes. So, when I joined the company I also joined as the

project physician for Paxil, which was a marketed product at the time.

Q. And what were your job responsibility with respect to Paxil?

11:43:32 A. It was similar to what we've described, ensuring that any new research that was being done--globally at that time was primarily Japan--that the protocols were appropriate for the outcomes being measured for monitoring of any safety events that occurred, for ensuring that the labeling was updated and 11:43:57 correctly based on any emergent data. Really collaborating with the teams for any events. If there was a manufacturing issue with the compound, even I would get involved in that as well.

Q. As part of your responsibilities, and we're going to -- 11:44:14 obviously, the jury has heard about this and we're going to talk a little bit more about it, did you have responsibility for reviewing the data derived from the adult suicidality analyses done by GSK and the FDA in 2006?

A. Yes. I was the project physician who reviewed that data, 11:44:32 correct.

Q. "Project physician," means you had the responsibility?

A. Yes. I had the medical governance accountability, yes.

Q. Now, we've heard the term "Paroxetine" and we've heard the term "Paxil." What is Paroxetine?

11:44:46 A. So, Paroxetine is what's called the INN or international

non-proprietory name for the chemical structure of Paxil, which I don't know if you have seen or not.

So, all it means is that that chemical structure is called Paroxetine, and, globally, that's the word that should be used for it. That's why it's considered non-proprietory, anyone can use that name "Paroxetine."

Q. And the jury has heard the term "Paxil." Was that the bran name for Paroxetine in the United States for a time?

A. Yes, "Paxil" was what called the brand name, yes.

Q. And there was also a product called Paroxetine, which was a generic product that was not manufactured by GSK, correct?

A. Yes; generic products not manufactured by GSK do exist.

Q. And one is called Paroxetine?

A. Yes.

Q. But when jury sees documents being sent to the FDA back in 189, 1991 that say "Paroxetine," that is the chemical name for the drug that later became marketed as Paxil in the United States?

A. That's correct.

Q. Now, in connection with your job responsibilities regarding Paxil, did you have to familiarize yourself with the results of clinical trials conducted on Paxil or Paroxetine before you joined the company?

A. Oh, absolutely. I had to understand the history of the development of the compound for couple of reasons: To

understand where --

THE COURT: Sir, just answer the questions.

THE WITNESS: Okay.

THE COURT: The question is - we'd like to keep it short and just answer.

Go ahead, sir.

BY THE WITNESS:

A. So, I think the answer was "yes."

BY MR. BAYMAN:

Q. Okay. Did you talk to people who were there at the time when analyses were conducted?

A. Yes.

Q. And did you review what the jury has heard, the NDA, the New Drug Application for Paxil?

A. Yes. I reviewed parts of that, yes.

Q. And did you review clinical trials that were conducted after the NDA on Paxil?

A. Yes, I did.

Q. And did you -- did you review and are you knowledgeable about what the testing on Paxil or Paroxetine shows about the medication's safety?

A. Yes.

Q. As part of your work, as part of your work in both academia and industry, have you gained familiarity with the FDA's regulation of prescription medicine such as Paroxetine?

A. Yes, I have.
Q. And does that include the process by which a manufacturer obtains FDA approval to market a medication?
A. Yes, it has.
11:47:31 Q. And does your experience include knowing the regulatory standards for including information in a medication's label?
A. Yes, it does.
Q. Have you personally been involved in drafting medication labeling?
11:47:47 A. Yes, I have.
Q. Have you done that with respect to Paxil or Paroxetine?
A. I have, yes.
Q. And have you had interactions with the FDA about changing labeling?
11:47:59 A. Yes, I have.
Q. And you are familiar with the process by which a manufacturer can change its product labeling after the product is already on the market?
A. Yes, I am.
11:48:11 Q. Did you also as part of your job responsibilities with respect to Paxil, did you familiarize yourself with the history of the labeling with respect to Paxil?
A. Yes. Typically for specific issues, but yes.
Q. Was one of those issues suicidality?
11:48:34 A. Yes, it was.

Q. And did you review the interactions and communications between the FDA and GSK regarding Paxil and the issue of suicidality before you had joined the company?
A. You mean when I was in clinical practice?
11:48:49 Q. No. No. No. When you joined the company, did you review the regulatory and labeling history of Paxil about events that happened before you came to the company?
A. I understand. Yes, I did. I knew when I joined the company that the suicidality analysis will be part of my
11:49:06 responsibility for interpretation. So I looked at what had come before it to understand the context.
Q. As a clinician who has been involved with drug labeling for more than a decade, do you have expertise in applying the regulations related to drug labeling and how to communicate
11:49:25 information to physicians through the label?
A. I would say yes, I do.
Q. And is that particularly true with respect to Paroxetine or Paxil?
A. Yes.
11:49:33 Q. And have your job responsibilities include speaking on behalf of the company about issues regarding Paxil and suicidality?
A. Yes, that's right.
Q. And what's your current position?
11:49:45 A. I did leave out the last promotion, I apologize for that.

My current position is Vice President in Medicine Development Leader now in the Dermatology Therapy Unit.

Q. So, just to summarize, you had responsibility for reviewing analysis data from Paxil and Paroxetine clinical trials, right?

11:50:12 A. Yes, that's correct.

Q. You also had responsibility at GSK for the design of some trials involving Paroxetine?

A. Yes; that's correct.

Q. And you were involved in preparing reports to the FDA

11:50:25 concerning data from Paroxetine clinical trials, including on the issue of suicidality?

A. Yes, that's correct.

Q. And you were involved in communicating with the FDA and to healthcare providers about the Paxil labeling?

11:50:39 A. Yes.

Q. And you were personally involved in the interactions between the company, GSK and the FDA, concerning the company's change to the Paxil labeling in 2006 and 2007 relating to a potential risk of suicidality in adult patients?

11:50:56 MR. WISNER: Objection, Your Honor. Leading. If he could not ask such open-ended questions.

THE COURT: Yeah, you're leading all the way through this.

MR. BAYMAN: Well, I'm just trying to shorten it, Your

11:51:04 Honor.

THE COURT: Well, shorten it. Get right to it. All this background is not necessary and not helpful.

MR. BAYMAN: Well, Your Honor, the jury heard a lot about Dr. Healy and about Dr. Glenmullen and their background and I think they ought to be able to hear the background of --

11:51:15

THE COURT: Well, they have. And we're delighted to have him here, but let's get on with it.

BY MR. BAYMAN:

Q. Have you offered scientific papers about Paxil and suicidality in peer-reviewed literature?

11:51:25

A. Yes, I have.

Q. Have you, as part of your experience, been involved in submitting new drug applications to FDA?

A. Yes, new drug applications, as well as what's happened called supplementary new drug applications.

11:51:45

Q. What is the regulatory standard for FDA approval of a new prescription medication?

MR. WISNER: Your Honor, at this time I would issue an objection. Specifically, I have no problem with this witness testifying factually about what GSK did in a regulatory perspective, but based on his deposition and his disclosure he tends to offer opinions about what the FDA would or would not do. He's never worked there, he's never had that perspective. And so, I would move to exclude any evidence or any opinions by this witness regarding what the FDA would or would not do.

11:51:59

11:52:18

MR. BAYMAN: I'm just asking him the regulatory standard. I didn't ask him what the FDA would or would not do.

MR. WISNER: He's not been proffered as a regulatory expert.

11:52:28 THE COURT: The regulatory standard is not within the range of what we want here. So I'm going to sustain that objection.

MR. BAYMAN: Your Honor, he's an expert in labeling.

THE COURT: Let's get to the issues, sir. I'm not

11:52:38 going to hold you back.

BY MR. BAYMAN:

Q. The FDA does have to review, when it seeks to approve a medicine, it also has to review the labeling, is that right?

A. Yes; when we submit a New Drug Application there is

11:52:53 proposed labeling, and that has to be agreed with the regulatory authority. And ultimately the FDA's labeling is what stands in the United States for the drug.

MR. WISNER: Objection. Move to strike his improper opinion.

11:53:06 THE COURT: No, it may stands. This is somewhat parallel to Dr. Ross.

MR. WISNER: Yes, but Dr. Ross worked at the FDA for 10 years.

THE COURT: That's true. And we aren't going to allow

11:53:16 the witness to testify as to the law, that is a matter for the

Court. So proceed.
BY MR. BAYMAN:
Q. Can a manufacturer sell a product in the United States without FDA approval of its label?
11:53:35 A. No.
Q. The jury has heard a lot about clinical trials and have heard from Dr. Gibbons from a statistical approach to that topic. I want to ask you about clinical trials from a clinician's perspective.
11:53:53 Are there different types of clinical trials that a drug company may conduct?
A. Yes, there's a number of different designs that can be used.
Q. What is the most robust type of clinical trial?
11:54:08 A. In terms of being able to have the evidence required for approval of a drug in the United States, what we call the pivotal studies or the key studies are the placebo-controlled studies, randomized placebo-controlled.
Q. As a clinician, why is it important to compare patients who
11:54:29 are in a trial exposed to a medicine versus to patients on placebo as compared -- comparing them to someone else?
A. Right. So what you're trying to do when you're studying a new medicine is, you have an idea of how to work to improve symptoms or outcomes in the disease. You also may have an idea
11:54:52 of how safety can work. But in order to understand whether

that's directly related to the medicine, you need a comparison group that is not getting that treatment.

And that's what we call the placebo group, meaning they're getting something that looks identical to the active
11:55:11 medicine but it has no medicine in it.

So, you can follow patients along to see in the placebo group, what are the sort of things that might just happen in the course of time. And in the drug group, what might happen that happen in the course of time but also change,
11:55:28 are there symptoms that get better or are there different side effects that you see.

So, in order to really understand what's happening with the medicine, you also have to understand what happens in the absence of the medicine to say whether or not there is an
11:55:40 association.

Q. But why is it important that it be placebo as compared to say another antidepressant?

MR. WISNER: Objection, Your Honor. This is becoming very cumulative.

11:55:49 THE COURT: It is cumulative. Sustained.

BY MR. BAYMAN:

Q. As a clinician, not a statistician, as a clinician, why is it important that patients are blinded in a clinical trial?

A. So "blinded" means that the patient doesn't know whether
11:56:06 they're getting the active medicine or the placebo, the

inactive medicine. And part of the reason for that is if a patient knows they're getting an active medicine, they may have certain expectations of either, "ah, I'm feeling better because I'm on an active medicine" or they may have a side effect where they think, "that's got to be due to the medicine" when it may not be. So, it's to try and kind of get rid of any bias that a patient may have.

11:56:25

On the flip side is, when we blind the investigators who are taking care of the patients, also don't know if they are on active treatment or a placebo, for the same reason, we want them to make objective assessments without any kind of bias or preconceived notions of what should happen to that patient.

11:56:42

Q. And as a former clinical investigator and someone who's analyzed a lot of clinical trial data, do you then compare events on Paxil versus on placebo to see if there's a difference?

11:56:58

A. Yes.

MR. WISNER: Objection, Your Honor. Again, I don't moon any disrespect, Dr. Kraus, but I really -- this is cumulative. These are almost the exact questions that were asked of Dr. Gibbons.

11:57:08

MR. BAYMAN: As a clinician, Your Honor.

THE COURT: Sir, I'm going to sustain it as a clinician. I don't see the reason for it. You're going to

11:57:19

have to persuade me that we should go over this again. We've been over it very thoroughly and very well, but I do not see the relevance here of that kind of a distinction. You're going to have to persuade me that there is some relevance to it.

11:57:33 BY MR. BAYMAN:

Q. Well, with respect to the safety of the medication that you're studying, not a statistical analyses but with respect to the safety of the medication you're studying, why is it important to compare a drug versus placebo, a sugar pill?

11:57:53 A. I think it's for the same reason --

MR. WISNER: I review my objection, Your Honor.

THE COURT: It's the same point. The same point. And we've heard testimony thoroughly, complete testimony on this topic, and I don't see the point in repeating it again and

11:58:04 taking up the time of the court or the jury to do so, without any criticism of the doctor.

We've heard it, Doctor, and we thank you very much.

Proceed, please.

BY MR. BAYMAN:

11:58:20 Q. Do placebo -- exposure to placebo, does that cause side effects?

A. It should not cause side effects, no, because there is no active medicine in the compound.

Q. And so that's what you are comparing?

11:58:34 A. You're comparing -- so, during the course of just going

through weeks in a study, say a study is 12 weeks, just naturally things can occur: Headaches, stomachache, getting a cold, things of that nature; that can all occur in a placebo.

So, if you have that occur also in the active arm, you
11:58:53 can make a judgment that, "well, this is something that just happens in the natural course of spending 12 beaks looking at somebody," right. However, the medicine itself may have its own effects.

Let's say, for example, a nausea or feeling sick to
11:59:08 your stomach happens more on the medicine, and you don't see it on the natural course as much on placebo. That's why you need a comparison to understand what might happen in the natural course of 12 weeks of a person's life versus those same 12 weeks upon a medicine that we're trying to understand.

11:59:24 Q. Now, in the Paxil -- the jury has heard the term "extension phase."

A. Yes.

Q. In the Paxil clinical trials, how long did some of those extension phases last?

11:59:34 A. Up to 52 weeks or a year.

MR. BAYMAN: Your Honor, permission to publish DX7035F. They've seen it before.

MR. WISNER: So, Your Honor, I think this is exactly the problem. This is the slide actually that was supposedly
11:59:52 created by Dr. Gibbons used in Mr. Bayman's opening statement.

I mean, this is the definition of cumulative. It is testimony about literally the same image.

MR. BAYMAN: No, I'm going into a different area, Your Honor.

12:00:05 THE COURT: Well, it sure looks the same. It is the same.

MR. BAYMAN: It's the same slide, but I'm asking different questions.

THE COURT: We've heard a great many answers about the

12:00:14 slide. I'll let you try.

MR. BAYMAN: Okay.

THE COURT: But if you go again to repeat the same thing and there's an objection, I'm going to sustain it.

MR. BAYMAN: I understand, Your Honor.

12:00:32 (Exhibit published to the jury.)

BY MR. BAYMAN:

Q. The jury has seen this. So, those Paxil patients in the extension phase, many of them -- did you just say many of them stayed on the drug for as long as 52 weeks longer?

12:00:50 A. That's correct.

Q. And do people stay on Paxil -- on placebo after the trial's end?

A. No; oftentimes people on placebo actually went to active drug as well. So, they also went in the uncontrolled extension

12:01:02 Paxil phase.

Q. The jury has heard the term through Dr. Ross's testimony about a relapse study. Are you familiar with the term "relapse study"?
A. Yes. Relapse prevention studies, yes.
12:01:20 Q. Have you created a graphic which would assist us to explain what a relapse study is?
A. Yes.
MR. BAYMAN: Your Honor, at this time permission to publish DX 70368.
12:01:38 MR. WISNER: No objection, Your Honor.
THE COURT: Is that among the papers I was given?
MR. BAYMAN: Yes, sir. It's on the inside. In your stack in there. I'm just jumping ahead. Trying to keep moving.
12:01:47 THE COURT: All right. I see it.
BY MR. BAYMAN:
Q. Just explain to the jury what a relapse study is.
A. Yes. And I'll start with the technical term and then I'll break it down.
12:01:58 We call these randomized withdrawal studies. So what does that mean? It means that the beginning of the study, before that randomization period, every person who meets the inclusion criteria, meaning they have the symptoms, severity of the depression or the anxiety disorder that we're studying
12:02:18 comes into the study, they meet that criteria, they all get

treated with the medicine, usually in what we call an open label. So, the patients know they're getting medicine because there is no comparison group.

Now, why is that done? The reason that's done in this
12:02:35 study is because we actually want to study persons who respond to the treatment, those who get better and have a response.

So, for those patients who have a response to the Paroxetine treatment, they actually then go to the randomization phase, which means, by chance, they either stay
12:02:55 on that medicine, Paxil, or they get withdrawn. So, that's why it's called the randomized withdrawal. And they actually go to placebo.

Now, you might say why are we doing that. What we want to see is if a person gets better on the medicine and
12:03:11 stays on it versus stopping it. Do they actually continue to do well.

So, that's why there's no control at the beginning, because we're just trying to get people to respond. And that's why there is a placebo in the other part, because we're trying
12:03:25 to see if you take the medicine away, what happens.

Q. But the -- after randomization, the patients don't know which medicine they're on, right?

A. That's right. In randomization, they're blinded. They don't know if they're staying on the medicine or going on to
12:03:40 the placebo or no medicine.

Q. Dr. Ross gave -- well, I'll move on.

Now, you mentioned --

MR. BAYMAN: You can take that, Mr. Holtzen.

BY MR. BAYMAN:

12:03:54 Q. You mentioned that other that randomized double-blind placebo-controlled trials GSK conducted other kinds of clinical trials. Just tell the jury, generally, what other kinds of trials GSK conducted.

A. Well, they concluded what are called active comparator

12:04:11 studies where you take Paxil, which was the new medicine at the time, and compare it with an established medicine.

So, back then there were things called the tricyclics. So, you've had the patients going to active medicine in each arm and compare whether one might be better than the other.

12:04:28 We talked about the randomized withdrawal. There are also studies that could be open label from the beginning to look at large numbers over large periods of time just to assess evidence continued efficacy and safety.

And I don't know if you want me to keep going, but

12:04:48 there can be something called crossover designs.

Q. Yes?

A. Where a patient may start on drug, and that same patient could go to placebo or to another medicine, so that's the crossover. Start on one, switch to another, and then you can

12:05:01 actually compare those two periods with that same patient to

say, okay, when they were on drug "X" this happened, and when they crossed over to drug "Y" this happened, and you can also cross over to placebo as well in those studies.

Q. In open-label studies, does the patient know what medicine they're taking?

12:05:19

A. Yes, open label means the patient knows that the clinical investigator who is evaluating them knows the medicine that they're on.

Q. And is there a placebo arm in these studies?

12:05:32

A. There is no placebo arm in those studies, no.

Q. The jury has heard the term from Dr. Healy "healthy-volunteer studies." What are healthy-volunteer studies?

A. Healthy-volunteer studies are when you're taking your medicine of interest, let's say in this instance Paxil, and it's being given to people without the disease that you're studying.

12:05:42

So, they don't have depression, they don't have anxiety disorders. And you might say, why are you giving the drug to healthy volunteers. The reasonable is this is usually done early in drug development, and there's a couple of reasons.

12:05:54

First, when you do something called "first time in human," you're trying to look at the potential dose that you might use in the disease population, and you look at how well

12:06:09

that dose is tolerated. So usually they start low and they go higher to see where's the safety.

We also use healthy volunteers to understand what's called the pharmacokinetics of the medicine. All that means
12:06:29 is, what are the blood levels that we see, how long does it take for the body to clear the medicine out of the system, and also what kind of organs are involved in clearing the medicine. Usually that's your liver, usually that's the kidneys, but you're actually able to figure that out.

12:06:47 And you also can use healthy volunteers to understand where the drug distributes in the body. Some drugs get accumulated in fat, for example. For a drug like Paxil that you want to make sure it gets to its target, the brain, you can actually study does it really get to the brain, those sorts os
12:07:08 things you do in healthy volunteers. And when you have that information, you can then really sensibly design the study for the disease.

Q. Now, in the United States are healthy volunteer studies done giving drugs to friends and colleagues in a hospital?

12:07:23 A. No; that would be considered unethical.

Q. Why not?

A. So, that again introduces bias into a study, and also it's strictly prohibited through our company policies. And having worked at UNC and having studies go through what's called an
12:07:43 institutional review board for ethics, it would never fly.

Q. Did GSK do healthy volunteer studies for Paroxetine prior to the time the drug was first approved?
A. Yes, we did.
Q. And are you familiar with those?
12:07:54 A. Yes.
Q. Were there any suicides during those healthy volunteer studies?
MR. WISNER: Objection. Move to strike. Cumulative. Almost an identical was asked of Dr. Gibbons yesterday.
12:08:07 MR. BAYMAN: I don't think so.
MR. WISNER: Almost verbatim, actually.
THE COURT: It may stand.
BY THE WITNESS:
A. There were no suicides in healthy volunteers.
12:08:14 BY MR. BAYMAN:
Q. Now, the jury has heard Dr. Healy say that there might have been a suicide in a Paroxetine healthy volunteer study. Are you familiar with that contention?
A. Yeah; I've heard that.
12:08:23 Q. Is Dr. Healy correct?
A. No.
Q. Why not?
A. My understanding is, with that subject, the suicide occurred some months after the study when there was no exposure
12:08:33 to medication nor in the study anymore.

Q. Dr. Healy said it was 3 months afterwards. How can you be sure that Paroxetine didn't have some lingering effect in that patient's body?

A. As I talked about before, those studies of photokinetics allow us to understand how long a drug will stay in the system.

12:08:50

For Paroxetine, it is a half life, meaning from the level you have when you take it every day, if you stop, when it gets to half that level of about 24 hours. So, in about five days the drug is out of the system, in general.

Q. Now, the jury has heard that GSK's clinical trials were not designed for the primary purpose of looking at whether Paroxetine or Paxil might induced suicidal thinking and behavior, is that true?

12:09:11

A. Can you ask that again, Mr. Bayman?

Q. Yeah. The jury has heard that GSK's clinical trials were not designed for the primary purpose of looking at whether Paroxetine or Paxil might induce suicidal thinking or behavior; is that true or accurate?

12:09:28

MR. WISNER: Objection, Your Honor. Move to strike Mr. Bayman's interpretation of what the jury has heard. I think he just ask him, does it induce suicidal thinking or behavior.

12:09:42

THE COURT: Sustained.

You can't argue it. You have to ask a specific. You got to tie it to something in the record.

12:09:52

Proceed that basis, please.
BY MR. BAYMAN:
Q. Dr. Ross has testified that GSK's clinical trials were not designed for the primary purpose of looking at whether Paroxetine might induce suicidal thinking or behavior, is that correct?
MR. WISNER: Again, I don't know how he would know the answer to that question unless he's reading the trial transcripts.
12:10:10 MR. BAYMAN: I'm not asking --
MR. WISNER: He just asked him if that's what he said. He said, "is that correct?"
MR. BAYMAN: I'm not asking him what he said.
THE COURT: Well, then if you're asking him what he said, I sustain the objection, because you can only go to the direct testimony and respond to it. You can't paraphrase it yourself, or restate it, or in any other way summarize it. You have to go direct to what he said, and in that fashion, he may respond to it.
12:10:34 BY MR. BAYMAN:
Q. Were GSK's clinical trials designed for the primary purpose of looking at whether Paroxetine might induce suicidal thinking and behavior?
A. No, the primary purpose of our clinical trials was to understand the efficacy and safety, which would include any

adverse event, including suicidality.

There were a couple of studies where suicidality was an outcome, so that was studied, but the vast majority of studies were not designed for that.

12:11:01 Q. Does that mean those trials aren't useful for in forming the question of whether Paxil or Paroxetine might be associated with an increase risk of suicide?

A. No; not at all.

Q. Explain that, if you would.

12:11:13 A. Right. So, the studies were designed to understand how well the drugs work for each of the diseases. And also, as we've talked about, looking at that placebo arm where you're just looking what happens over time, whether or not there are differences between side effects in that drug versus just

12:11:33 watching a patient over time.

And in a disease like depression where one of the key symptoms is actually suicidality and suicidal thinking, that actually can lead to the diagnosis, it can happen naturally as part of the disease course.

12:11:50 So, it's very important to understand and compare against those two groups, but for any adverse events that's true.

So, those studies that we conducted, you know, for the 2007 and '6 analysis, it was about 15,000 total subjects, we

12:12:06 were able to look, side by side, and actually look at the

adverse events, including suicidality. And they can inform us whether or not there might be an association with drug versus placebo. So, they're still informative even though they weren't designed for that purpose.

12:12:24 And one thing to think about is, or to remember, is in reporting adverse events, very serious events like a suicide attempt or a suicide, they tend to get reported; whereas, maybe milder things may be missed.

So, we're confident that these events would've been 12:12:41 caught in our clinical trials, and the comparisons we've made have been valid in helping us understand that issue.

Q. And when you say they tend to get reported, you mean by the patient to the investigator?

A. Oh, yeah.

12:12:52 Q. And do the investigators actually conduct -- you mentioned these rating scale assessments. Do they conduct them at the time with the patient or do they fill them in later after the patient is finished with trial?

A. You conduct them at the time with the patient.

12:13:14 Q. Now, did GSK ever conduct a study of any drug where the primary outcome was designed to make someone suicidal?

A. No.

Q. Why wouldn't you do that?

A. As I just indicated, depression itself is associated with 12:13:31 suicidality. It would be unethical to try and develop a study

to put patients already at risk at increased risk. And, in fact, when we do these studies suicidality is monitored closely, including sometimes being a disqualification for coming to the study as having suicidal behavior to ensure that
12:13:59 if a patient went on placebo, for example, no treatment, that they aren't at risk of harming themselves during this study.
Q. Now, you mentioned '05 and '06, and that study has been mentioned in this trial. Did GSK ever conduct clinical trials in patients who were at particularly high risk for suicide?
12:14:19 A. Yes, we had. Those two studies.
Q. Could you tell us about this.
A. Yes. So, '05 and '06 were designed to assess Paroxetine versus a placebo in the background of kind of psychotherapy. So, there was treatment ongoing even though a drug and a
12:14:39 placebo were given in patients who had high risk of suicidal behavior.

In fact, the inclusion criteria included having suicidal behavior prior to coming in. And we had had, and we may talk about, evidence that Paroxetine reduces depression,
12:14:58 that it reduces suicidal thinking as measured by rating scales. And the concept was if we were to look at these high-risk patients, which were called at that time intermittent brief depression, could the suicidality actually improve with treatment versus placebo.

12:15:14 In those studies, we didn't find that. We found there

was no difference in the overall rate of suicidal behaviors in those studies.

So, no indication that Paroxetine reduced it, no indication that it increased it in this highly vulnerable
12:15:30 population that has suicidality as core part of their disease.

Q. How did those results help answer the question as to whether Paxil or Paroxetine might induce suicide?

A. Well, if you think about it, if you posit that there's a bona population to suicidality, you might think a population
12:15:48 that already enriched for wanting to harm themselves might actually be at an increased risk. We didn't see that. So, it didn't show any evidence of an increase in suicidality at that time.

Q. Would -- did those studies drown out a signal of suicide in
12:16:11 Paroxetine or Paxil?

A. In the 2006 analysis?

Q. No. No. Just with those studies, would they drown out a signal for suicide if you included those in the analysis?

A. No. No.

12:16:20 Q. And were the patients in '05 and '06 were those the kind of patients where you would expect to see suicidality?

A. Yes. In fact, when we talk about that inclusion criteria, how you get into a study, they had to have suicidality as inclusion criteria.

12:16:42 Q. And are there regulations that require companies to submit

information to the FDA about clinical trials?
A. I'm sorry, Mr. Bayman. Can you ask that again?
Q. Are there regulations that require companies to submit information to FDA about clinical trials?
12:16:56 A. Yes.
Q. And did GSK have to prepare quarterly and annual reports that address safety issues for Paroxetine or Paxil?
A. Yes. We have to provide periodic safety updates, and additionally we have to provide, before the drug is approved,
12:17:16 annual updates, and additionally after it's approved annual New Drug Application updates.
Q. And what are included in those updates? What kinds of information?
A. We provide any new safety information that's emerged. We
12:17:34 summarize any changes that may have occurred in the label. We provide what clinical studies are ongoing. Concluded and completed different studies all over the globe to the FDA.
Q. If there were suicide and suicide attempts that occurred during those clinical studies, would that information be
12:17:54 reported to the FDA?
A. Yes. So, deaths are reported, of course.
Q. What about suicide attempts?
A. Yes, they'd be forward as adverse events within the context of these studies.
12:18:03 Q. Now, based on your experience as someone working for the

company and someone who has conducted trials yourself, when the FDA requests data from placebo-controlled portions of a clinical trial, what's your understanding of they're looking for?

12:18:25 MR. WISNER: Objection. Speculation.

THE COURT: Sustained. Covered.

BY MR. BAYMAN:

Q. You've seen the FDA use the term placebo-controlled portion of clinical trials in its communications with GSK over the

12:18:36 years?

A. Yes.

Q. And if -- if placebo-controlled portions of clinical trials included more than just when there is a concurrent placebo group, would that be the kind of information that the FDA was

12:18:59 seeking in 2006 when it did its analysis?

A. No.

MR. WISNER: Objection. Speculation.

THE COURT: Sustained.

BY MR. BAYMAN:

12:19:05 Q. You were involved in responding to the FDA's request in 2006 to submit clinical trial data, correct?

A. Yes. When I joined the company, we were still submitting the data to the FDA, that's correct.

Q. And did you, in fact, respond, you and your colleagues,

12:19:26 respond to their request in 2006 to submit clinical trials to

the FDA?
A. Yes. FDA initially gave a request to all companies, including GSK, wanting to study the question of whether or not antidepressants may have a role in being associated with
12:19:43 suicidality as compared to placebo.
So, they requested that we provide them with short-term studies, so acute studies. So, kind of the randomized control ones that you had heard about, that had over 30 patients to make sure that there is at least enough patients
12:20:03 so there wasn't single-site or small-study effects, and that these be less than 17 weeks. The only wanted the placebo-controlled portions, and actually provided a list to the company from our New Drug Application that we've talked about of studies that they thought met that criteria.
12:20:24 Q. What was your understanding, based on your experience, of what you were to submit when the FDA requested the placebo-controlled portions of the clinical trials?
MR. WISNER: Objection. Asked and answered.
THE COURT: It's been covered. Sustained.
12:20:37 BY MR. BAYMAN:
Q. Well, can we put back up 7036, the relapse study.
(Brief pause).
(Exhibit published to the jury.)
BY MR. BAYMAN:
12:20:52 Q. Doctor, looking at this relapse study design which you

explained earlier to the jury, would the acute phase of the relapse study when patients were on Paroxetine, would that be placebo-controlled?

A. No, those patients would not be included in that request.

12:21:09 MR. BAYMAN: Mr. Holtzen, put up 70369, the clinical trials. The one we showed the jury.

(Brief pause).

(Exhibit published to the jury.)

BY MR. BAYMAN:

12:21:18 Q. Would open label extension phases be placebo-controlled?

A. No. In this graphic, only the controlled phase would be included.

Q. I want to talk to you now about the population of patients that made up the clinical trials on Paroxetine or Paxil that

12:21:50 supported GSK's initial New Drug Application that was ultimately approved in 1992.

Are you familiar with that?

A. Yes.

MR. BAYMAN: Your Honor, at this point I would like

12:22:10 permission to publish demonstrative exhibit 7036-10.

MR. WISNER: Andy -- I'm sorry, Mr. Bayman, why don't we just do -12, it's the same diagram. I assume you plan to use that. Does that work?

MR. BAYMAN: Yeah. I'll just jump ahead, if that's

12:22:38 okay with you.

MR. WISNER: Yes.

MR. BAYMAN: Let's put up then DX7036-12.

(Exhibit published to the jury.)

BY MR. BAYMAN:

12:22:55 Q. Do you see that graphic, Doctor?

A. Yes, I do.

Q. Can you describe for the jury the types of Paroxetine clinical trials that supported the initial FDA approval.

A. So, as I stated before, the sorts of studies that support

12:23:12 approval are the pivotal placebo-controlled studies.

So, in this graphic they're kind of the middle ones, the placebo-controlled studies, the control phase that would contribute to the approval.

Q. No, I'm talking about the initial, back in early '90s, what

12:23:32 type of studies were submitted for approval. Were they just placebo-controlled?

A. Oh, every single study we did would be submitted. The FDA would base their decision on efficacy and safety based on the placebo portion.

12:23:43 Q. Okay. And so how many in the clinical trials that supported the FDA's initial approval of Paxil, how many -- how many patients were included?

A. It was -- as you can see here, we have approximately 3,000 Paroxetine exposed patients in the studies that you have listed

12:24:08 here.

Q. And then looking at this graphic -- looking at -- so, you got almost 3,000 patients who have been studied on Paxil or Paroxetine?
A. Right. At the first approval. Clearly, there's been more since then.
Q. Right. And then if you look at, if you will -- and out of the total population, that was -- was that almost 5,000 patients?
A. Out of the total population, yes.
Q. Yes. And if you look at how many patients were in the Paroxetine placebo in active-controlled patients, do you see that?
A. Yes.
Q. How many patients received Paroxetine in a randomized placebo-controlled trial?
A. 921 subjects.
Q. And how many received it in an active control trial?
A. 1096.
Q. And how many total placebo patients were in these studies?
A. 554.
Q. And then how many patients were given other medications, what we call active control?
A. 1151.
Q. Now, based on your experience and expertise, if you were going to make an assessment about the -- whether the medication

is associated, as a clinician, with an increase risk of suicide, which groups would you compare?

A. As we discussed, that would be in the controlled phase of the placebo-controlled portion.

12:25:44 Q. So which -- which on the graphic?

A. In that middle group in the graphic.

THE COURT: All right. We will recess now for our luncheon break.

(The following proceedings were had out of the presence of the jury in open court:)

[redacted]

(Luncheon recess taken from 12:30 o'clock p.m. to 1:30 o'clock p.m.)

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I CERTIFY THAT THE FOREGOING IS A CORRECT TRANSCRIPT FROM THE RECORD OF PROCEEDINGS IN THE ABOVE-ENTITLED MATTER

/s/Blanca I. Lara April 6, 2017

12:26:59